REMARKS/ARGUMENTS

Claims 1-4, 12-15, 21-38, 43, 46 and 47 are pending in the application. Claims 43, 46 and 47 are withdrawn.

Claim 14 stands rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The Examiner states that the claim depends on claim 12 which recites numerous fluorescent proteins and it is unclear whether all said proteins have identical amino acid sequences. If not, the Examiner states that it would be unclear what is the referenced base amino acid sequence. In response, Applicants submit that claim 14 relates only to Green Fluorescence Protein, as it refers the protein as "GFP". Thus, the rejection should be withdrawn.

Claims 1-4, 12-15, 21, 23-38, 43, 46 and 47 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The Examiner states that it is unclear if in claim 1(a) the modified cytochrome C is restricted to human source. In response, Applicants have amended the claims to adopt the Examiner's suggestion. Thus, the rejection should be withdrawn.

Claims 1-4, 12-15, 21-38, 43, 46 and 47 stand rejected under 35 U.S.C. §112, first paragraph, as containing new matter. At issue is the proper reference to the position of the substituted amino acid in the claims. While Applicants argued previously that the convention of numbering the amino acid sequence positions for cytochrome C does not count the first methionine, the recited SEQ ID NO: 2 starts from the first methionine. Therefore the reference in the previous claims of K72 substitution should be changed to K73 substitution in the claims. The Examiner found the above argument unpersuasive.

Applicants further submit that SEQ ID NO: 2 contains a proline at position 72, a lysine at both position 73 and 74. Thus there is no lysine at position 72 of SEQ ID NO: 2. While Applicants inadvertently used a conventional numbering system for cytochrome C, no confusion is likely here. Further, in the amino acid sequences where Applicants present a K72A mutation (See, e.g., Figure 9, SEQ ID NO: 6), the Alanine is in fact at position 73 if the initiation methionine is counted as the first amino acid. Here, the lysine at position 74 is present. Applicants submit that based on the sequence information from SEQ ID NO: 2 and SEQ ID NO: 6, it is clear that there is support for an amino acid substitution at K73, as currently claimed, and there is no K72 in SEQ ID NO: 2. No new matter is introduced.

Claims 1-4, 12-15 and 21-38 stand rejected under 35 U.S.C. §103(a), as being unpatentable over Los et al. in view of Evans et al. further in view of Kluck et al. Applicants respectfully disagree.

In response, Applicants first submit that Los et al. does not teach a cytochrome C-reporter fusion protein construct that includes a cytochrome C and a fluorescent protein. Los et al. merely discloses an antibody-based method for detecting and quantifying cytochrome C which is present in cells or released from cells. The method, as described on page 38 of Los et al., involves preparing cellular lysates or extracellular fractions, immunoprecipitation with an anti-cytochrome C antibody, immunoblotting and quantification using horseradish peroxidase conjugated secondary antibodies. Thus Los et al. does not teach, suggest or motivate the use of a fluorescent protein which forms part of a cytochrome C-reporter fusion protein construct and which can be used in a living cell.

Applicants also submit that although Kluck et al. teaches modification of K73, it relates to an in vitro process only. The shortcomings of the Kluck et al. teachings are discussed in the present application (see page 4, line 11 to page 5 line 4) where the uncertainties of moving from an in vitro to an in vivo system are highlighted. The current application, on the other hand, relates to a cytochrome C-reporter fusion protein construct which targets the mitochondria and has a reduced ability to induce apoptosis in a living cell (see claim 1).

Applicants submit that none of the references, even if combined, teach the claimed cytochrome C-reporter fusion protein construct as exemplified by claim 1, or any of the subject matter in the dependent claims.

Applicants submit that the 35 U.S.C. §103(a) rejection of the claims should be withdrawn in view of the amendments and the above arguments.

Applicants assert that the claims are in allowable form and earnestly solicit the allowance of claims 1-4, 12-15, 21-38, 43, 46 and 47.

Early and favorable consideration is respectfully requested.

Respectfully submitted,
GE Healthcare Bio-Sciences Corp.
By: /Yonggang Ji/
Yonggang Ji
Reg. No.: 53,073
Agent for Applicants

GE Healthcare Bio-Sciences Corp.
Patent Department
101 Carnegie Center
Princeton, New Jersey 08540

Tel 1: (609) 514-6371
Tel 2: (732) 980-2875

I hereby certify that this correspondence is being uploaded to the United States Patent and Trademark Office using the Electronic Filing System on February 10, 2011.

Signature: /Melissa Leck/

Name: Melissa Leck

T:\Legal\Pat_Dept\IP Dept\Response to Office Action\PA\2011\PA0394 (10FEB2011).doc